

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MGH/PC/P10959PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 03444	International filing date (day/month/year) 06/09/2000	(Earliest) Priority Date (day/month/year) 07/09/1999
Applicant THE UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:

1-6, 18, 22, 36

2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 13493 A (UMANSKY SAMUIL ;MELKONYAN HOVSEP (RU); LXR BIOTECHNOLOGY INC (US)) 2 April 1998 (1998-04-02) page 7, line 26 -page 8, line 2; claim 44 claim 44 ---	1-6, 18, 22, 36
X	WO 97 39357 A (UNIV LELAND STANFORD JUNIOR ;UNIV JOHNS HOPKINS (US)) 23 October 1997 (1997-10-23) page 10, line 30 -page 12, line 25 ---	1-6, 18, 22, 36
X	EP 0 882 793 A (SMITHKLINE BEECHAM CORP) 9 December 1998 (1998-12-09) page 12, line 44 -page 13, line 52; claims 16-19 ---	1-6, 18, 22, 36
X	EP 0 879 881 A (SMITHKLINE BEECHAM CORP) 25 November 1998 (1998-11-25) page 10, line 55 -page 11, line 47 ---	1-6, 18, 22-36
P, X	EP 0 943 684 A (SMITHKLINE BEECHAM PLC) 22 September 1999 (1999-09-22) page 2, line 11 - line 19 paragraph '0053! ---	1-6, 18, 22, 36
A	WO 98 54325 A (US HEALTH) 3 December 1998 (1998-12-03) page 2, line 29 - line 31 page 23, line 9 - line 22 page 25, line 21 - line 29 ---	1-6, 18, 22-36
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 747 336 A (BUCKLEY NOEL J ET AL) 5 May 1998 (1998-05-05) column 5, line 22 - line 28 column 6, line 27 - line 31 ---	1-6, 18, 22-36
A	US 5 871 940 A (FENG GUOPING ET AL) 16 February 1999 (1999-02-16) column 2, line 20 - line 22 claim 1 ---	1-6, 18, 22-36
P, A	EP 0 955 364 A (INST MOLECULAR BIOLOGY AND BIO) 10 November 1999 (1999-11-10) the whole document -----	1-6, 18, 22-36

Patent Family Annex

Information on patent family members

International Application No

PCT/GB 00/03444

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9813493	A	02-04-1998	AU	4651397 A	17-04-1998
			EP	0932678 A	04-08-1999
WO 9739357	A	23-10-1997	AU	2664797 A	07-11-1997
EP 0882793	A	09-12-1998	US	5994098 A	30-11-1999
			CA	2230963 A	02-12-1998
			JP	11075866 A	23-03-1999
EP 0879881	A	25-11-1998	CA	2221837 A	23-11-1998
			JP	11004698 A	12-01-1999
			JP	2000102395 A	11-04-2000
EP 0943684	A	22-09-1999	JP	11253183 A	21-09-1999
WO 9854325	A	03-12-1998	AU	7704498 A	30-12-1998
US 5747336	A	05-05-1998	NONE		
US 5871940	A	16-02-1999	US	5593862 A	14-01-1997
EP 0955364	A	10-11-1999	NONE		

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-6, 18, 22, 36 in part

Screening assay, method for identifying or producing compounds having a potentially pesticidal activity, comprising a sequence selected from SEQ ID No. 1 (Frizzled gene) specific fragments thereof, homologues thereof, or the encoded proteins thereof.

Inventions 2-544 claims 1-6, 18, 22, 36 in part

As for invention 1, each invention 2-544 comprising one SEQ ID. selected from SEQ. ID. No. 2-429 and 784-898.

Inventions 545-902: Claims 1-6, 18, 22-36 in part

As for invention 1, each invention 545-902 comprising one SEQ ID. selected from SEQ ID's 430-783 and 899-902 as well as the corresponding isolated polynucleotide fragment per se.

A PCT application shall comply with the requirement of unity of invention (Article 3(4)(iii) PCT). Rule 13.1 prescribes this requirement as being fulfilled if the application relates to one invention only. If the application relates to more than one invention, as is presently the case, then they must be so linked as to form a single general inventive concept. Such a link is, in view of the state of the art, not present. In consequence the application is considered to relate to at least 902 separate inventions of which the one first mentioned in the claims has been searched. The ISA invites the applicant, pursuant to Article 17(3)(a), to pay 901 additional search fees.

The application as a whole sets out to solve the problem of identifying essential genes of an organism in order to predict pesticide targets, drug target, herbicide targets etc. The definition of a gene being essential has been arbitrarily determined by the applicant so as to include "semi-lethal" mutations. An example solution to this problem with respect to *Drosophila* as presented by the present application (not claimed) is to mutagenise *drosophila* by P-element insertions and to select lethal and semi-lethal mutants which are subsequently characterised by cloning and sequencing DNA surrounding the P-elements. This results in DNA sequences similar, or identical, to known sequences as well as DNA sequences to yet unknown genes. The application further proposes to solve the problem of identifying further essential genes of other organisms, which are not yet known per se, by comparing a gene with the so identified allegedly novel sequences (Claims 26-28).

The single general concept linking all claimed inventions is that identification of essential genes of an organism leads to the identification of drug targets, pesticide targets, herbicide targets etc. It is common knowledge in e.g. the pesticide field that many, if not all, pesticides provide a certain biochemical activity. If this activity affects an essential function of the organism it will die or it will be more vulnerable to its environment or to disease or attack. The

formulation of this concept follows logically from common knowledge in the field of e.g. pesticides. This single general concept can hence not be the single general inventive concept of Rule 13.1 PCT.

The closest prior art at hand is either of W097/39357 (p. 10, l. 30 -p-12, l. 25), US5871940 (col. 2, l.20-22) or US574336 (col. 5, l. 22-28; col. 6, l. 27-31)

W097/39357 disclosed the binding relation between Wnt and the Wnt receptor (= Dfz2 = frizzled gene; cf p. 7, lines 1-4). A screening for drug candidates is done by expressing the essential gene Dfz2 on the surface of cells and monitoring modulation of interaction between Wnt and the receptor. It is noted that the "frizzled gene" gene has been identified in the description by matching with one of the 902 sequences (SEQ ID No. 1).

US5871940 disclosed the tipE mutant gene of drosophila melanogaster as a gene which mutation leads to the semi lethal condition of paralysis at temperature above 38°. The DNA sequence of the gene has been disclosed as well as a method of identifying agents which modulate the physiological activity of the translated gene product using the gene. It is noted that the tipE gene has been identified in the description by matching with one of the 902 sequences (SEQ ID No. 39).

Also US5747336 (05.05.99) disclosed an essential gene and proposed it as a target for drug screening (human muscarinic acetylcholine esterase receptor). It is noted that the muscarinic acetylcholinic receptor has been identified in the description by matching with one of the 902 sequences (SEQ ID No. 3).

Because no common technical effect has been linked with a structural feature present in all 902 SEQ. ID's, or in the so identified essential genes, the broadest possible problem to be solved is to provide further DNA sequences derived from essential genes serving as possible targets for drug screening pesticide screening, herbicide screening etc.

The solutions proposed thereto are the separate sequences 1-902. If these sequences would be linked so as to form a single general inventive concept than the condition of Rule 13.2 must be met, i.e. there must be a same or corresponding special technical feature shared by all 902 SEQ ID's or in the so identified essential genes, which makes up the contribution to the state of the art.

Neither the claims nor the list of sequences or the application as a whole discloses a technical feature or a technical effect linked thereto which is the same for all 902 inventions and which makes up a contribution over the state of the art (i.e. over US5871940). A suggested link is the status of the sequences as relating to essential genes which are possible drug targets, pesticide targets etc. But such link constitutes merely a reformulation of the problem to be solved: "To identify essential genes of an organisms to select drug targets, pesticide targets etc." This problem is an obvious desideratum which, as such, cannot make up a contribution over the state of the art, if any. A further suggested link is the fact that these sequences can be used to

formulate the assay of claim 1. It is evident, however, that the method features of the assay in claim 1 are generalizations of all technical features of the state of the art assays mentioned in the description. It is immediately clear that the assays used in the description are state of the art assays and can hence not be considered to contribute to a same or corresponding special technical feature making up a contribution over the state of the art (See page 46, last paragraph, page 49, first paragraph etc.). This leaves as only technical feature(s) structural features of the separate SEQ. ID's in claim 1.

It is noted that the reason for a gene being essential lies in the uniqueness of the combined features of the gene. Essentiality cannot be considered as a true technical effect of the individual features of a sequences. The "effect" of being essential cannot be derived from a technical effect attributable to any same or corresponding features which a gene shares with other genes. If there are technical features of a gene which it shares, by way of the same or corresponding structural features, with 901 other genes then this feature alone can never render a gene essential.

The requirement of unity of invention is not met and each single SEQ ID together with its use has to be searched and evaluated separately for being novel and inventive. And it follows from the above reasoning that the possible non-obviousness of one of the 902 SEQ ID's cannot render the other 901 inventive.

The invention related to the SEQ ID No. 1 (the "frizzled like genes") was the subject of the first search.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 12-14 , 16 and 17 encompass methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition insofar the application sufficiently discloses or supports such compounds in the sense of Articles 5 and 6 PCT.

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 12-14, 16,17

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box 3.

Claims Nos.: 7-17, 19-21

Present claims 7-17, 19-21 relate to an extremely large number of possible compounds. In fact, the claims contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

Moreover, these compounds are defined by reference to a desirable characteristic or property, namely that they can be identified by the method of the screening assay claims. Claims 7-17, 19-21 cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search has been carried out for these claims.

In addition it is noted that these claims can also not describe the subject-matter for which protection can be sought (Article 6 PCT, first sentence). It is highly likely that any known pesticide e.g. those listed in "The pesticide manual" (ISBN 0 948404 79 5) falls within the scope of claim 7. The claims do not allow any discrimination between known and novel subject-matter and the skilled person will always be in doubt if

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

his compound falls under the claim or not.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.